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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/507,239	02/18/2000	Hugh S. Keeping	04930-028001	9324

7590 12/19/2001

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EXAMINER
BECKERLEG, ANNE M 14

ART UNIT	PAPER NUMBER
1632	5/23/02
DATE MAILED: 12/19/2001	

Please find below and/or attached an Office communication concerning this application or proceeding.



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09/507,239	02/18/2000	Hugh S. Keeping	04930-028001	9324

7590 05/24/2002

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BECKERLEG, ANNE M

ART UNIT	PAPER NUMBER
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Office Action Summary	Applicant No.	Applicant(s)
	09/507,239	KEEPING ET AL.
	Examiner	Art Unit
	Anne M Beckerleg	1632

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on 03 October 2001.
- 2a) This action is FINAL. 2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 38-59 is/are pending in the application.
- 4a) Of the above claim(s) 50-59 is/are withdrawn from consideration.
- 5) Claim(s) _____ is/are allowed.
- 6) Claim(s) 38-49 is/are rejected.
- 7) Claim(s) _____ is/are objected to.
- 8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) The proposed drawing correction filed on _____ is: a) approved b) disapproved by the Examiner.
 If approved, corrected drawings are required in reply to this Office action.
- 12) The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) All b) Some * c) None of:
 1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. _____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) The translation of the foreign language provisional application has been received.
- 15) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) <u>10</u> . | 6) <input type="checkbox"/> Other: _____ |

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DETAILED ACTION

Applicant's amendment and response to the restriction/election requirement has been entered. Claims 1-37 have been canceled and new claims 39-59 have been entered. Claims 38-59 are pending in the instant application. An action on the merits follows.

Election/Restriction

Applicant's election without traverse of Group III, claim 38, in Paper No. 11 is acknowledged. The applicant states that new claims 39-59 are drawn to the subject matter of the elected invention. However, only new claims 39-49 are actually drawn to the subject matter of Group III, claim 38, which recite a method of inducing differentiation of a bone marrow cell comprising contacting the cell with bone morphogenic protein-6. Claims 50-59 are drawn to patentably distinct subject matter which was not claimed in the original set of claims filed with the instant invention. The new subject matter comprises methods of inducing the differentiation of a bone marrow stromal cell by culturing the cell in the presence of a transfected cell expressing a BMP. The subject matter of claims 50-59 is classified in class 435, subclass 325 and 320.1. Further, transfected cells are substantially different in structural, physical, biological, and functional properties than a bone morphogenic protein. In addition, the method of claim 38 does not utilize the transfected cells of claim 50 and vice versa. Thus, the inventions are distinct

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because of their recognized divergent subject matter, different classification, and different search requirements. Applicant's election without traverse of the subject matter of Group III, claim 38 has been noted above. Therefore, in view of the patentably distinct nature of the invention of claims 50-59 from that of the elected invention, claims 50-59 are withdrawn from consideration as being drawn to subject matter non-elected without traverse in paper no. 11. Claims 38-49 are currently under examination at this time.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 38, 39, 42-44, 47-49 are rejected under 35 U.S.C. 102(b) as being anticipated by Yamaguchi et al. (1996) Biochem. Biophys. Res. Comm., Vol. 220, 366-371. The applicant claims a method of inducing the differentiation of a bone marrow stromal cell comprising contacting the cell with bone morphogenic protein 2, 4, or 6. The applicant further claims said methods wherein the cell is a mammalian cell, or wherein the cell was previously frozen.

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Yamaguchi et al. teaches the differentiation of murine bone marrow stromal cells comprising contacting the cells during *in vitro* tissue culture with human bone morphogenic protein (BMP) 2, or BMP-4, or BMP-6 (Yamaguchi et al., page 366, abstract, and page 369, Figure 3). Yamaguchi et al. further teaches that the cell used in these experiments were obtained from the RIKEN Cell Bank in Tsukuba, Japan. At the time of filing, it was well known that cell lines are stored by freezing the cells in liquid nitrogen. Frozen cell lines are capable of being shipped around and subsequently thawed at the destination for use in biological assays. Thus, by using a cell line obtained from a cell bank, Yamaguchi et al. teaches the use of cells which have been previously frozen. Therefore, by teaching all the elements of the claims, Yamaguchi et al. anticipates the instant invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to

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the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103© and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claims 38-49 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 6,281,195 (8/28/01), hereafter referred to as Rueger et al., in view of Yamaguchi et al. (1996) Biochem. Biophys. Res. Comm., Vol. 220, 366-371. The applicant claims a method of inducing the differentiation of a bone marrow stromal cell comprising contacting the cell with bone morphogenic protein 2, 4, or 6. The applicant further claims said method wherein the cells are human, or canine cells. It is noted that the claims read on the differentiation of bone marrow stromal cells *in vivo* and *in vitro*.

Rueger et al. teaches methods of inducing bone formation in a mammal comprising providing directly to the defect locus in a bone an osteogenic protein such as BMP-2, BMP-4, or BMP-6 (Rueger et al., columns 54-55, claims 1, 11 and 12). Rueger et al. further teaches that the osteogenic protein can be administered to numerous types of mammals including dogs, rabbits, and humans (Rueger et al., columns 3-4, and columns 25-30).

Rueger et al. differs from the instant invention in not specifically teaching that the osteogenic protein comes in contact with bone marrow stromal cells such that the stromal cells differentiate. It is noted, however, that it was well known at the time of filing that bone marrow contains bone marrow stromal cells. Yamaguchi et al. further supplements Rueger et al. by

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teaching that bone marrow stromal cells are specifically induced to differentiate by bone morphogenic proteins such as BMP-2, BMP-4, and BMP-6. In particular, Yamaguchi et al. teaches the differentiation of murine bone marrow stromal cells comprising contacting the cells during *in vitro* tissue culture with human bone morphogenic protein (BMP) 2, or BMP-4, or BMP-6 (Yamaguchi et al., page 366, abstract, and page 369, Figure 3). Therefore, in view of the known composition of bone marrow, and the teachings of Yamaguchi of the ability of BMPs to induce bone marrow stromal cell differentiation, it is inherent based on the properties of bone morphogenic proteins that the method of administering BMPs directly to a bone defect to induce bone formation would include the differentiation of bone marrow stromal cells. The applicant is reminded that reliance upon inherency is not improper even though rejection is based on Section 103 instead of Section 102. *In re Skoner, et al.* 186 USPQ 80 (CCPA).

Alternatively, based on the activity of BMP-2, BMP-4, and BMP-6 in inducing the differentiation of bone marrow stromal cells as taught by Yamaguchi et al., and the known composition of bone marrow, it would have been *prima facie* obvious to the skilled artisan that the direct administration of BMP-2, BMP-4, or BMP-6 to a bone, as taught by Rueger et al., would result in the differentiation of resident bone marrow stromal cells with a reasonable expectation of success.

No claims are allowed.

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Any inquiry concerning this communication from the examiner should be directed to Anne Marie S. Beckerleg, Ph.D., whose telephone number is (703) 306-9156. The examiner can be reached Mon-Thurs and every other Friday from 9:30-7:00. If the examiner is not available, the examiner's supervisor, Karen Hauda, can be reached at (703) 305-6608. General inquiries should be directed to the group receptionist whose phone number is (703) 308-0196. The technology center fax number is (703) 308-4242, the group fax number is (703) 308-8724.

Dr. A.M.S. Beckerleg

**A.M.S. BECKERLEG.
PATENT EXAMINER**

